REMARKS

Claims 26-50 are currently pending in this application. Claims 42-50 have been withdrawn from consideration as directed to non-elected subject matter. Claims 26-33 and 35 have been amended and new claim 51 has been added in the above amendments. Hence, claims 26-41 and 51 will be pending and under examination upon the entry of this amendment.

New claim 51 has been added to more particularly recite unique features of the polypeptides of this invention. In particular, the new claim specifies that these polypeptides: (i) elicit a T-cell dependent immune response when conjugated to a T-independent antigen (for example, a polysaccharide); and (ii) comprise an amino acid sequence from the N-terminal portion of an IgA1 protease from either *Neisseria meningitidis*, *Neisseria gonorrhoeae* or *Haemophilus influenzae*. These features are all described in the present application as originally filed, as summarized in the Table, *infra*. Claims 26-33 and 35 have been amended to depend from new claim 51. Claim 26 has also been amended, without prejudice or admission, to delete the recitation of "at least 80% homologous."

Limitation	Support
• elicits a T-cell dependent immune response to a T-independent antigen.	• page 3 at lines 1-3; • page 7 at 19-24; • Examples 5 and 6 at pages 17-19.
• comprises an amino acid sequence from IgA1 of *Neisseria meningitidis*.	• page 3 at lines 11-12; • page 4 at line 12; • page 4 at lines 27-28.
• comprises an amino acid sequence from IgA1 of *Neisseria gonorrhoeae*.	• page 4 at line 31.
• comprises an amino acid sequence from IgA1 of *Haemophilus influenzae*.	• page 3 at line 12.

For the reasons explained above, all of the amendments are fully supported by the application as filed and do not constitute new matter. Entry of the amendments is therefore respectfully requested.

The Rejections For Enablement Under 35 U.S.C. 112, First Paragraph, Should Be Withdrawn:

Claims 26-41 have been rejected under the first paragraph of 35 U.S.C. § 112 as not being enabled. In particular, the Office Action alleges that this application "provides no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different amino acid substitutions and the nature and extent of the changes that can be made." See, the second paragraph starting at page 4 of the Office Action. For this reason, the Examiner contends that this application does not reasonably provide enablement for peptides that are "at least 80 or 85% identical to" the particular sequences recited in the pending claims – *i.e.*, the sequences of SEQ ID NOS:1-5.

In response to this rejection Applicants respectfully point out that, contrary to what is stated in the Office Action, this application as filed does provide guidance by which a person of ordinary skill in the art can readily determine which amino acid residues can be changed in a polypeptide of the invention without causing a detrimental effect. The specification explains that polypeptides of the invention, when conjugated to a T-independent antigen (for example, a polysaccharide) are capable of eliciting a T-cell dependent immune response to that antigen. For example, see the specification as filed from line 30 on page 2 to line 5 on page 3; see also at page 7 on lines 19-24. The application even provides assays (*e.g.*, in Examples 5 and 6 at pages 17-19 of the specification as filed) by which a polypeptide can be tested to determine whether that polypeptide, when conjugated to a T-independent antigen, will produce a T-cell dependent immune response to that antigen. These assays are straight forward and, given the teaching of this application, they can be routinely performed by persons having ordinary skill in the art.

These features of Applicants' invention are clarified in new claim 51, which has been introduced with this amendment. Specifically, new claim 51 particularly recites that the claimed

p lypeptide is "abl to elicit a T-cell dependent immune respons to a T-independent antigen [for example, a polysaccharide] when conjugated to [that] antigen." Rejected claims 26-41 have all been amended, without prejudice or admission, so that they depend either directly or indirectly from new claim 51. Moreover, Applicants note that claim 26 has also been amended (again, without prejudice or admission) so that it only specifies polypeptides that are "identical to an amino acid sequence" recited in that claim, and not polypeptides that are "at least 80% homologous" to those sequences.

As explained above, the present application as filed does provide guidance by which a skilled artisan can identify polypeptides specified in the claims, including variants of the particular amino acid sequences. Although some experimentation may be necessary to identify particular variant polypeptides, such testing is straight forward and routine for persons of ordinary skill in the art given the teaching of this application. As such, the experimentation cannot be considered undue. The test for enablement is whether a person who is reasonably skilled in the art could make and use the claimed invention without undue experimentation, using the disclosure in the patent coupled with information that was known when the patent application was filed. *United States v. Telectronics, Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). The proper test is not, therefore, whether any experimentation would be necessary, but instead, if experimentation would be necessary, whether it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). The fact that experimentation may be complex does not necessarily make it undue. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983). See, also, *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

For all of the above reasons, Applicants submit that the pending claims are fully enabled by the specification as filed, and respectfully request that the rejections for enablement be withdrawn.

The Written Description Rejections Under 35 U.S.C. 112, First Paragraph, Should Be Withdrawn:

Claims 26-41 have also been rejected under the first paragraph of 35 U.S.C. § 112 as lacking adequate written description in the application as filed. In particular, the Office Action alleges that the application only describes the polypeptide sequences set forth in SEQ ID NOS:1-5 and "is not

commensurate in scope with the claims drawn to hom logous sequences with no recited function." See, the Office Action in the first paragraph at page 7.

At the outset, Applicants wish to again respectfully point out that the polypeptides of this invention do have a specific function. Namely, when conjugated to a T-independent antigen (for example, a polysaccharide), the polypeptides are capable of eliciting a T-cell dependent immune response to that antigen. As noted above, this function is described in the application as filed, for example, from line 30 on page 2 to line 5 on page 3. See also, at page 7 on lines 19-24. The application additionally describes assays (*e.g.*, in Examples 5 and 6 at pages 17-19) by which the function of these polypeptides can be verified.

New claim 51 has been introduced with this amendment to particularly recite this function. Pending claims 26-41 have also been amended so that they depend, either directly or indirectly, from new claim 51. Hence, all of the pending claims particularly specify that the polypeptides of this invention: (i) are derived from the IgA1 protease amino acid sequence of either *Neisseria meningitidis*, *Neisseria gonorrhoeae*, or *Haemophilus influenzae*; and (ii) are "able to elicit a T-cell dependent immune response to a T-independent antigen [*e.g.*, a polysaccharide] when conjugated to said antigen."

The Manual of Patent Examining Procedure (M.P.E.P.) provides, at Section 2163 *et seq.*, that "[a]n adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the invention had possession of the claimed invention." M.P.E.P. § 2163.II.A.3(a). Such characteristics may include, *inter alia*, "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Id.*

As explained above, the pending claims all define a specific functional characteristics of the claimed polypeptides which is described in the application as filed. Moreover, the functional characteristic of these polypeptides is shown to correlate to a particular structure – they are all polypeptides comprising at least 40 amino acid residues of an IgA1 protease (a protein that is already well known in the art) from any of the species of *Neisseria meningitidis*, *Neisseria*

gonorrhoeae and *Haemophilus influenzae*. For these reasons Applicants submit that pending claims of this application are all adequately described in the specification as filed, and respectfully request that the written description rejection be withdrawn.

The Obviousness Rejections Under 35 U.S.C. 103 Should Be Withdrawn:

Claims 26-32 have been rejected under 35 U.S.C. § 103(a) as being obvious, and therefore unpatentable, over the combined teachings of Lomholt *et al.*, *Mol. Microbiol.* (1995) 15:495-506 ("Lomholt I"); Poulsen *et al.*, *Infect. Immun.* (1989) 57:3097-3105 ("Poulsen"); Lomholt, *APMIS* (1996) Suppl. 62:5-28 ("Lomholt II"); and International Patent Publication No. WO 90/11367 by Kilian *et al.* ("Kilian"). Each of these references is said to describe an IgA1 protease from various species (including *H. influenzae* and *Neisseria gonorrhoeae*) and/or fragments thereof. In addition, Poulsen and Lomholt II are said to teach that the N-terminal part of mature IgA1 protease has been evolutionary conserved. Lomholt II and Kilian also allegedly teach that IgA1 protease or fragments thereof may be useful as vaccines, for immunizing against disease caused by IgA producing bacteria.

The pending claims of this application specify polypeptides that are derived from the N-terminal portion of an IgA1 protease from various species. However, unlike the peptide fragments allegedly taught in the cited references, the pending claims of this application particularly specify peptides that "elicit a T-cell dependent immune response to a T-independent antigen [for example, a polysaccharide] when conjugated to said antigen." See, in particular, new claim 51 introduced in this amendment.

By contrast, the references cited by the Examiner only describe, at the very best, fragments of an IgA1 protease that are useful as epitopes to generate antibodies against that protein. None of the references cited in the Office Action describes any IgA1 fragment that, when conjugated a polysaccharide or other "T-independent antigen," elicits a T-cell dependent immune response to that T-independent antigen. Although some of the cited references (*e.g.*, Kilian) may teach that such fragments can be used in vaccines, such vaccines are only said to be ones for "immunizing against

allergic diseases, gonorrhoea ***and other diseases caused by IgA protease-producing bacteria***." See, Kilian at lines 15-20 on pag 1 (emphasis added). Hence, these references can only describe IgA1 fragments that generate an immune response against the IgA1 protease itself.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. M.P.E.P. § 2143.03. Even if it can be shown that the skilled artisan would have been motivated to combine and/or modify cited references, it must also be shown that the modification or combination of those references would teach or suggest every element of the invention so that the invention, as a whole, would be apparent to the skilled artisan. As explained above, none of the references cited by the Examiner teaches or suggests any peptide (much less an IgA1 peptide) that when conjugated a polysaccharide or other "T-independent antigen," elicits a T-cell dependent immune response thereto. Hence, the present application does not establish a *prima facie* case for obviousness under 35 U.S.C. § 103(a). Applicants therefore respectfully request that the rejections for obviousness be withdrawn.

Conclusion:

For the reasons stated above, Applicants believe that the Examiner's rejections of the pending claims have been overcome and that the claims are in condition for allowance. Accordingly, the withdrawal of all objections and rejections, and reconsideration of the application are respectfully requested. The Examiner is, moreover, invited to contact the undersigned

representative if he believes that it may advance prosecution of this application. An allowance is earnestly sought.

Respectfully submitted,

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